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Date: January 14, 2005 Monica L. Thomas

PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of: David J. Yang et al.	Group Art Unit: 1615
Application Serial No.: 10/024,678	Examiner: Fubara, Blessing M.
Filed: December 18, 2001	Atty. Dkt. No.: UTXC:681US
For: Board of Regents, The University of Texas System	Title: LOCAL REGIONAL CHEMOTHERAPY AND RADIOTHERAPY USING IN SITU HYDROGEL

APPEAL BRIEF

Commissioner for Patents
Washington, D.C. 20231

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APPEAL BRIEF

MS Appeal Brief
Commissioner of Patents
Washington, D.C. 20231

Sir:

Appellants hereby submit an original and two copies of this Appeal Brief to the Board of Patent Appeals and Interferences in response to the final Office Action dated October 14, 2004 (the "Action"). The Notice of Appeal is filed herewith.

The fee for filing this Appeal Brief is $250.00 and is enclosed herewith. Please date stamp and return the attached postcard as evidence of receipt.

I. REAL PARTY IN INTEREST

The real parties in interest are the assignee, Board of Regents, The University of Texas System, and its licensee, Cell<Point, LLC.

II. RELATED APPEALS AND INTERFERENCES

There are no related appeals or interferences.

III. STATUS OF THE CLAIMS

Claims 1-125 were originally filed on December 18, 2001 in this case, which claims priority to U.S. Provisional Application Serial No. 60/256,514, filed on December 18, 2000.

In response to a Restriction Requirement dated March 26, 2003, Appellants filed an amendment on April 23, 2003 in which claims 14 and 15 were amended, and claims 23, 46, 69, and 71-125 were canceled. In response to a species election in the Restriction Requirement, Appellants elected the specific method of claim 1 and the specific therapeutic agent being the drug cisplatin.

Following an Office Action mailed July 15, 2003, a Response was filed on November 17, 2003 wherein claims 1, 5, 8, and 9 were amended, claims 4, 6, and 7 were canceled, claims 18-22, 24-45, 47-68, and 70 were withdrawn, and new claims 126-127 were added.

An Office Action was mailed February 24, 2004, and a Response was filed on June 30, 2004 in which claims 1 and 2 were amended and new claim 128 was added.

Claims 1-3, 5, 8-22, 24-45, 47-68, 70, and 126-128 were pending in the Final Office Action dated October 14, 2004, and claims 18-22, 24-45, 47-68, and 70 were withdrawn. Thus, claims 1-3, 5, 8-17, and 126-128 are pending on appeal and are the subject of this appeal brief.

A copy of the pending claims is attached as Appendix 1.

IV. STATUS OF AMENDMENTS

There are no outstanding amendments in the pending claims.

V. SUMMARY OF THE CLAIMED SUBJECT MATTER

The present invention concerns *in situ* delivery of a therapeutic agent to a localized region by administering a polymer and a cross-linker from separate containers (see at least paragraphs **[0016]** and **[0017]** of the specification). In particular, the polymer and the cross-linker are administered from separate containers to allow formation of a cross-linked polymer *in situ* at the localized region, which cross-linked polymer comprises the therapeutic agent (see at least paragraphs **[0016]** and **[0017]**). Separation of the polymer and cross-linker prevents premature polymerization such that polymerization occurs after the therapeutic agent and polymer and cross-linking components are delivered, thereby preventing polymerization within the delivery apparatus, for example.

In specific embodiments, separate administration of the polymer composition and the cross-linker to the localized region utilize syringes comprising the first and second containers. (see at least paragraph **[0017]**). In additional specific embodiments, the polymer is, for example, a polysaccharide, such as an alginate, for example (see paragraph **[0022]**). In another specific embodiment, the cross-linking agent is a salt of a divalent cation, such as Ca^{2+}, for example (see at least paragraph **[0022]**). Furthermore, the therapeutic agent may be a drug, such as cisplatin, for example (see at least paragraph **[0022]**).

VI. GROUNDS OF REJECTION TO BE REVIEWED ON APPEAL

Claims 1-3, 5, 8, 9, 13-16, 126 and 127 are rejected under 35 U.S.C. §102(b) as allegedly being anticipated by U.S. Patent No. 5,989,215 ("Delmotte").

Claims 1-3, 8-11, 13-17, and 126-128 are rejected under 35 U.S.C. §103(a) as allegedly being unpatentable over U.S. Patent No. 5,945,100 ("Fick").

VII. ARGUMENT

A. Substantial Evidence Required to Uphold the Examiner's Position

As an initial matter, Appellants note that findings of fact and conclusions of law by the U.S. Patent and Trademark Office must be made in accordance with the Administrative Procedure Act, 5 U.S.C. § 706(A), (E), 1994. *Dickinson v. Zurko*, 527 U.S. 150, 158 (1999).

Moreover, the Federal Circuit has held that findings of fact by the Board of Patent Appeals and Interferences must be supported by "substantial evidence" within the record. *In re Gartside*, 203 F.3d 1305, 1315 (Fed. Cir. 2000). In *Gartside*, the Federal Circuit stated that "the 'substantial evidence' standard asks whether a reasonable fact finder could have arrived at the agency's decision." *Id.* at 1312.

Accordingly, it necessarily follows that an Examiner's position on Appeal must be supported by "substantial evidence" within the record in order to be upheld by the Board of Patent Appeals and Interferences.

B. Issue under 35 U.S.C. §102(b)

1. Claims 1-3, 5, 8, 9, 13-16, and 126-127 are Novel

Claims 1-3, 5, 8, 9, 13-16, and 126-127 are rejected as allegedly lacking novelty. The Action contends that the claims are anticipated by Delmotte. Appellants traverse the rejection.

The Examiner has the burden to make a *prima facie* case of lack of novelty, which requires noting how the reference meets each and every limitation of the claims. The Examiner has not met this burden.

Delmotte appears to teach separate administration of fibrinogen and thrombin to a tumor site to prevent premature fibrin formation. This does not teach the elements of Appellants' claims, given that it does not teach separate administration of a polymer and a cross-linker. Fibrinogen is a monomer, not a polymer. This is not explicitly stated in Delmotte but rather is inherent therein, and fibrinogen being a monomer is well-known in the art.

Furthermore, thrombin is not a crosslinker; in fact, it acts as a protease (col. 6, line 41) to proteolytically cleave the fibrinogen monomers thereby to produce fibrin monomers. Specifically, commercial kits described in the Background of Delmotte itself illustrates the fibrinogen/thrombin/fibrin relationship:

> "after mixing of components, the fibrinogen is proteolytically cleaved by thrombin and thus converted into fibrin monomers. Factor XIII is also cleaved by thrombin into its activated form (FXIIIa). **FXIIIa cross links** the fibrin monomers to form a three-dimensional network commonly called "Fibrin Gel.""(emphasis added).

Thus, Factor XIII, the cross-linker (see also col. 12, lines 38-43 of Delmotte), is cleaved by thrombin into its activated form (FXIIIa) to permit cross-linking of the fibrin monomers to form a polymerized fibrin gel (col. 2, lines 4-13).

Therefore, Delmotte teaches administration of fibrinogen, which is not a polymer, and administration of thrombin/calcium, which is not the cross-linker. Delmotte administers a monomer (fibrinogen) and a facilitating agent (thrombin/calcium) for preparing the monomer and for activating the cross-linker (Factor XIIIa), whereas Appellants administer a polymer (such as alginate) and a cross-linker (such as calcium).

Thus, the Examiner has failed to meet the Examiner's burden of demonstrating a *prima facie* case of anticipation.

2. Claims 1- 3, 5, 8, 9, 13-16 and 126-127 are Separately Patentable

The present invention is not anticipated under 35 U.S.C.§ 102(b) in view of Delmotte. In particular, the Examiner has not explained how all of the elements of each of the claims have been taught in Delmotte. Therefore, the rejection of these claims must be reversed.

a) Claim 2 stands rejected under 35 U.S.C.§ 102(b)

Claim 2 recites a method of dispensing a therapeutic agent in situ to a localized region in an individual comprising administering to the region a polymer composition that comprises a biocompatible polymer, a cross-linking composition that comprises a cross-linker, and the therapeutic agent, wherein the biocompatible polymer and the cross-linking composition are administered to allow formation of a cross-linked polymer *in situ* at the localized region, which cross-linked polymer comprises the therapeutic agent, and wherein the biocompatible polymer and the cross-linking composition are administered to the localized region from separate containers, wherein a first container comprises the biocompatible polymer and a second container comprises the cross-linking composition and wherein the biocompatible polymer comprises the therapeutic agent.

The Examiner fails to show where the elements of claim 2 are taught in Delmotte, and in the event that claim 1 falls, claim 2 is separately patentable and not anticipated by Delmotte.

b) Claim 3 stands rejected under 35 U.S.C.§ 102(b)

Claim 3 comprises claim elements that are not identified by the Examiner in Delmotte, and therefore a *prima facie* case of novelty has not been met. Claim 3 is separately patentable if claim 1 should fall, and it is not anticipated by Delmotte.

c) Claims 5, 8, and 9 stand rejected under 35 U.S.C.§ 102(b)

Claims 5, 8, and 9 are separately patentable because they contain elements that the Examiner has failed to identify in Delmotte, and a *prima facie* case of novelty has not been presented. In the event that claim 1 falls, claims 5, 8, and 9 are separately patentable and not anticipated by Delmotte.

d) Claims 13-15 stand rejected under 35 U.S.C.§ 102(b)

The Examiner fails to show where in Delmotte all of the elements of claims 13-15 are taught, and therefore fails to establish a *prima facie* case of novelty. Thus, these claims are separately patentable from claim 1 and are not anticipated by Delmotte.

e) Claim 16 stands rejected under 35 U.S.C.§ 102(b)

Claim 16 is separately patentable because all of its claim elements have not been identified by the Examiner as to their location in Delmotte and, thus, a *prima facie* case has not been met. In the event that claim 1 falls, claim 16 is separately patentable and not anticipated by Delmotte.

f) Claim 126 stands rejected under 35 U.S.C.§ 102(b)

Claim 126 is separately patentable, as all of its elements are not identified by the Examiner as to their teaching in Delmotte. Therefore, a *prima facie* case of novelty has not been met by the Examiner. In the event that claim 1 falls, claim 126 is separately patentable and not anticipated by Delmotte.

g) Claim 127 stands rejected under 35 U.S.C.§ 102(b)

The Examiner also fails to identify where in Delmotte all of the claim elements of claim 127 are taught and therefore does not present a *prima facie* case of novelty. Claim 127 is separately patentable in the event that claim 1 falls, and it is not anticipated by Delmotte.

C. Issue under 35 U.S.C. §103(a)

1. Claims 1-3, 8-11, 13-17, and 126-128 are Not Obvious

Claims 1-3, 8-11, 13-17, and 126-128 were rejected under 35 U.S.C. § 103(a) as allegedly being obvious in view of Fick. Appellants traverse this rejection.

Appellants assert that the Examiner fails to make a *prima facie* case rejection under 35 U.S.C. §103(a). The reference must teach or suggest every element of the claimed invention. When the Examiner relies on a single reference as modified to teach the claimed invention, there must be some suggestion for all of the elements. The Fick reference is admittedly missing an element of the claims—the delivery from different containers—and the Examiner has failed to adequately explain on the record where Fick suggests that this element is present.

MPEP §2143 states that to establish a *prima facie* case of obviousness, there must be some suggestion or motivation in the reference or in the knowledge generally available to a skilled artisan to modify the reference, and the reference must teach or suggest all of the claim limitations. The Examiner fails to make a *prima facie* case of obviousness because there is no suggestion or motivation to modify the reference, and furthermore because the Examiner fails to identify where in Fick Appellants' claims are taught or suggested and fails to show where in the prior art this knowledge is available. Motivation is a factual question that cannot be resolved in "subjective belief and unknown authority." *In re Lee*, 277 F.3d 1338, 1344 (Fed. Cir. 2002).

Moreover, the Examiner is improperly combining the reference with what she is saying is well-known in the art, and although the Examiner has had at least one opportunity to supply an affidavit as to what is well-known in the art, the Examiner has not done so. The reference by itself is insufficient to suggest Appellants' claims, and the Examiner has not explained how one would modify the reference based on the prior art. If the Examiner is relying on personal knowledge to support the finding of what is known in the art, the Examiner must provide an affidavit or declaration setting forth specific factual statements and explanation to support the finding. See 37 CFR §1.104(d)(2).

As already stated herein, Appellants' claims regard methods that dispense a therapeutic agent in a cross-linked polymer formulation through delivery of the polymer and cross-linker separately to the site *in situ* thereby delaying polymerization until the polymer and cross linker come into contact at a specific location, such as a tumor site or just prior to arriving at the tumor site. The present invention overcomes deficiencies in the art ***including*** Fick, wherein there is no

teaching or suggestion to keep the polymer and crosslinker separate until *in situ* administration. However, plain reading of Fick, which is silent on delivery from different containers, implicitly teaches mixing of the polymer and cross-linker prior to its delivery.

Fick concerns problems of insufficient penetration and/or reduced backflow and diversion through a point of entry related to introduction of a material in a tumor (see Abstract and col. 4, lines 46-51). Fick makes no mention of there being a potential complication upon mixing of the polymer and crosslinker. Furthermore, given that Fick does not realize the problem inherent therein, the two solutions will become polymerized within the delivery vessel. Recognizing that Fick is wholly concerned with sufficient penetration of a tumor, one of skill in the art would assume that special steps to keep the polymer and cross linker separate would be unnecessary. This important parameter is never mentioned or suggested in Fick, and a skilled artisan would not be motivated to address it.

Moreover, Fick is entirely prophetic. Fick does not describe how to implement the invention and more importantly does not even recognize that a significant problem exists. Thus, there is no teaching to keep the solutions separate, and one of skill in the art who does not seek to innovate would not find it necessary and obvious to keep the solutions separate.

The person of ordinary skill in the art is an objective legal construct presumed to think along conventional lines without undertaking to innovate, whether by systematic research or by extraordinary insights. *Life Technologies, Inc. v. Clontech Laboratories, Inc.*, 224 F.3d 1320, 56 U.S.P.Q.2d 1186 (Fed. Cir. 2000), citing *The Standard Oil Co. v. American Cyanamid Company,* 774 F.2d 448, 227 U.S.P.Q. 293 (Fed. Cir. 1985), which states the following:

> The statutory emphasis is on a person of ordinary skill. Inventors, as a class, according to the concepts underlying the Constitution and the statutes that have created the patent system, possess something--call it what you will--which sets them apart from the workers of ordinary skill, and one should not go about determining obviousness under § 103 by inquiring into what patentees (i.e., inventors) would have known or would likely have done, faced with the revelations of references. ***A person of ordinary skill in the art is also presumed to be one who thinks along the line of conventional wisdom in the art and is not one who undertakes to innovate***, whether by patient, and often expensive, systematic research or by extraordinary insights, it makes no difference which (emphasis added).

Thus, in the absence of the Fick teaching otherwise, a skilled artisan could simply mix the two solutions and quickly administer them to the tumor, such as through a catheter (see Abstract and col. 4, lines 51-55). Therefore, there would be no motivation to modify Fick based upon knowledge in the art, especially since Fick himself does not acknowledge any potential deficiencies of his methods.

The Examiner alleges that it would be inherently obvious to keep the polymer and cross linker solutions separate. This is an inaccurate statement. A skilled artisan looks at the reference and does what he is told from the reference. *Life Technologies, Inc. v. Clontech Laboratories, Inc.*, 224 F.3d 1320, 56 U.S.P.Q.2d 1186 (Fed. Cir. 2000), citing *The Standard Oil Co. v. American Cyanamid Company,* 774 F.2d 448, 227 U.S.P.Q. 293 (Fed. Cir. 1985). The Examiner's allegation assumes that one of skill in the art is required to innovate, which is an improper supposition because the skilled artisan performs the methods taught or suggested therein, and the teaching of the reference is completely silent on delivery hazards.

The absence of teachings in Fick concerning delivery problems indicates that Fick did not recognize the problem, and if Fick himself does not recognize the problem, then it is presumptuous of the Examiner to state that is obvious to a skilled artisan to keep them separate. It is well-settled case law that absence of recognition of a problem is strong evidence against obviousness of a reference. Of particular relevance in the present matter, courts have long held that to render a claimed invention obvious, the prior art must recognize the source or existence of the problem in the first place. For example, the U.S. Supreme Court has held that in the case of a known problem, the identification of the source of that problem is patentable, even where the solution is obvious once the source is known. *Eibel Process Co. v. Minnesota & Ontario Paper Co.*, 261 U.S. 45, 68 (1923). Similarly, a "patentable invention may lie in the discovery of the source of a problem even though the remedy may be obvious once the source of the problem is identified." *In re Sponnoble*, 160 U.S.P.Q. 237, 243 (C.C.P.A. 1969). A corollary to these principles is where the prior art fails to recognize the existence of a problem in the first place. In this regard, the CCPA has held that it is improper to conclude that an invention is obvious absent evidence that one of skill would have recognized that an underlying problem existed. *In re Nomiya*, 184 U.S.P.Q. 607 (CCPA 1975).

As noted in passing above, the caselaw strongly supports a conclusion of non-obviousness in the present case. The Supreme Court, in *Eibel Process*, noted that the discovery of the source of a known problem is strong evidence of non-obviousness:

> ... we must not lose sight of the fact that one essential part of Eibel's discovery was that the trouble causing the defective paper product under high machine speed was in the disturbance and ripples some ten feet from the discharge and that they were due to the unequal speeds of stock and wire at that point and could be remedied by equalizing the speeds. The invention was not the mere use of a high or substantial pitch to remedy a known source of trouble. ***It was the discovery of the source not before known and the application of the remedy for which Eibel was entitled to be rewarded in his patent.***

Eibel, 261 U.S. at 67-68. (emphasis supplied). See also *Sponnoble*, 160 U.S.P.Q. at 243 ("It should not be necessary for this court to point out that a patentable invention may lie in the discovery of the source of a problem even though the remedy may be obvious once the source of the problem is identified.").

Perhaps most relevant to our situation is the *Nomiya* case, where the CCPA, relying on the principles of *Eibel Process* and *Sponnoble*, held that invention is found in the recognition of a previously unknown problem:

> If, as appellants claim, there is no evidence of record that a person of ordinary skill in the art at the time of appellants' invention would have expected the problem in the IGFET to exist at all, ***it is not proper to conclude that the invention which solves this problem, which is claimed as an improvement of the prior art device, would have been obvious to that hypothetical person of ordinary skill in the art.*** This significance of evidence that a problem was know in the prior art is, of course, that knowledge of a problem provides a reason or motivation for workers in the art to apply their skill to its solution. Logically, the instant situation is one step removed from the circumstances illustrated by [Eibel Process], where the rippling in paper produced on Fourdrinier paper-making machines was known, but the source of the problem was not.

Nomiya, 184 U.S.P.Q. at 612-13. (emphasis added)

In the present case, as in *Nomiya*, the ***Action fails to present substantial evidence that those of skill recognized the existence or source of the problem associated with the mixing of the two solutions.***

As noted in MPEP 2144.03 and in keeping with *In re Zurko* (258 F.3d 1385, 59 USPQ2d 1697 (Fed. Cir. 2001)), an assessment of basic knowledge and common sense that is not based on any evidence in the record lacks substantial evidence support, and the Examiner has provided no evidentiary support for the assertion that one of skill in the art would recognize the problem in Fick that Appellants' invention in fact solves. The Examiner must provide specific factual findings predicated on sound technical and scientific reasoning to support his or her conclusion of common knowledge. *In re Chevenard*, 139 F.2d 713, 60 USPQ 241 (CCPA 1943). *In re Soli*, 317 F. 2d 941, 945-946, 137 USPQ 797, 800 (CCPA 1963). Moreover, if the Appellant adequately traverses the Examiner's assertion of official notice, the Examiner must provide documentary evidence in the next Office Action if the rejection is to be maintained. See 37 CFR §1.104 (c)(2) and *Zurko*, 258 F.3d at 1386, 59 USPQ2d at 1697. Again, if the Examiner is relying on personal knowledge to support the finding of what is known in the art, the Examiner must provide an affidavit or declaration setting forth specific factual statements and explanation to support the finding. See 37 CFR §1.104(d)(2).

As stated, there is no motivation for separate containers because Fick does not imply or state that it would be preferable that they should be kept separate. Fick teaches a catheter for administration of the composition and makes no suggestion or indication that it should be bi-compartmental, for example. Fick is remiss in suggesting a problem is even possible, so one of skill in the art based on what little is provided in Fick would use a catheter to apply the solutions, for example by quickly delivering them in the catheter following their mixture.

Obviousness may not be established using hindsight or in view of the teachings or suggestions of the inventor. *Para-Ordnance Manufacturing, Inc. v. SGS Importers International, Inc.* 73 F.3d 1085, 37 USPQ2d 1237 (Fed. Cir. 1995), *cert. denied*, 519 U.S. 822 (1996). To establish *prima facie* obviousness of a claimed invention, all of the claim limitations must be taught or suggested by the prior art. *In re Royka*, 490 F.2d 981, 180 USPQ 580 (CCPA 1974). There must be a teaching or suggestion to make the claimed limitations, and Applicants remind the Examiner that the level of skill in the art cannot be relied upon for suggestion. *Al-Site Corp. v. VSI Int'l Inc.*, 174 F.3d 1308, 50 USPQ2d 1161 (Fed. Cir. 1999). Thus, Applicants assert that the Office has not established a *prima facie* case of obviousness to reject the claims under 35 U.S.C. §103. *In re Vaeck*, 947 F.2d 488, 20 USPQ2d 1438, (Fed. Cir. 1991).

Finally, even if Fick had suggested that the compositions should be administered separately, ***which it does not***, there is no suggestion that the administration should be from separate containers, as delineated in Applicants' claim 1. The administration could be from the same containers at separate times, such as successive administration of one after the other through the catheter. Given that Fick is entirely prophetic, there is no motivation for the skilled artisan to do anything other than, for example, mix the solutions and quickly deliver them from the same container.

The Examiner does not point to anywhere in Fick that suggests implicitly or that states explicitly that there is motivation to keep the compositions separate. Where applicable, the findings ***should clearly articulate which portions of the reference support any rejection***. Explicit findings on motivation or suggestion to select the claimed invention should.....be articulated in order to support a 35 U.S.C. 103 ground of rejection. *In re Dillon*, 919 F.2d at 693, 16 USPQ2d at 1901; *In re Mills*, 916 F.2d 680,683, 16 USPQ2d 1430,1433 (Fed. Cir. 1990). Obviousness can not be based on "common knowledge and common sense of a person of ordinary skill in the art without any ***specific hint or suggestion in a particular reference***." *In re Lee* 277 F.3d 1338, 61 USPQ2d 1430 (Fed. Cir. 2002) (emphasis added). Given that Fick does not suggest or teach separation of the compositions, Applicants respectfully assert that the Examiner is inferring this parameter from the claimed invention, which is inappropriate. The reference must be viewed without the benefit of impermissible hindsight vision afforded by the claimed invention. *Hodosh v. Block Drug Co., Inc.*, 786 F.2d 1136, 1143 n.5, 229 USPQ 182, 187 n.5 (Fed. Cir. 1986).

In fact, given the lack of teaching or suggestion regarding separate administration of the polymer/cross-linker in Fick, the two components therein may be mixed at a temporal and/or physical distance from the localized region in a patient and subsequently applied by catheter to the region. Applicants overcome such problems that would manifest with the methods of Fick in which there is no such teaching, suggestion or motivation to keep the compositions separate; Appellants' invention prevents such pre-mixing issues such that solidification does not occur at the time of injection. Applicants' invention ensures that solidification occurs after the components have been injected by using different administration parameters, including administration more or less simultaneously from separate containers. The configuration in Fick does not guarantee that polymerization occurs afterward, and it is deleterious for polymerization

to occur during the administration, such as within a syringe. ***This problem is not recognized in Fick, so there would be no motivation to overcome it.*** In the specific embodiments of the present claims, Applicants devised a way to avoid this issue by injection from two separate containers wherein mixing occurs in the localized region, such as in the tumor.

Thus, these claims are not obvious in view of the Fick reference.

2. Claims 1-3, 8-11, 13-17, and 126-128 are Separately Patentable

The evidence of record overwhelmingly indicates that the present invention is non-obvious under 35 U.S.C. §103(a) over Fick. In particular, the Examiner has failed to make a *prima facie* case of obviousness, since the Examiner has failed to state where all of the elements of claims 1-3, 8-11, 13-17, and 126-128 are taught or suggested by Fick. Therefore, the requirements for establishing a *prima facie* case of obviousness are not met, and the rejection of these claims must be reversed.

a) Claim 2 stands rejected under 35 U.S.C. §103(a)

Claim 2 is separately patentable because the Examiner fails to state where all of the claim elements have been taught or suggested. Therefore, the requirements for establishing a *prima facie* case of obviousness have not been met. In the event that claim 1 falls, claim 2 is separately patentable and not obvious in light of Fick.

b) Claim 3 stands rejected under 35 U.S.C. §103(a)

Claim 3 is separately patentable because no *prima facie* case of obviousness has been made, given that the Examiner fails to state where all of the claim elements have been taught or suggested. Thus, in the event that claim 1 falls, claim 3 is separately patentable and not obvious in light of Fick.

c) Claims 8 and 9 stand rejected under 35 U.S.C. §103(a)

Claims 8 and 9 are separately patentable because the Examiner fails to state where all of the claim elements have been taught or suggested. Therefore, the requirements for establishing a *prima facie* case of obviousness have not been met, and in the event that claim 1 falls, claims 8 and 9 are separately patentable and not obvious in light of Fick.

d) Claims 10 and 11 stand rejected under 35 U.S.C. §103(a)

Claims 10 and 11 are separately patentable from claim 1 because the Examiner fails to state for these claims where all of the elements have been taught or suggested. Thus, the

requirements for a *prima facie* case of obviousness have not been met in this case, and should claim 1 fall, claims 10 and 11 are separately patentable and not obvious in light of Fick.

e) Claims 13, 14, and 15 stand rejected under 35 U.S.C. §103(a)

Claims 13, 14, and 15 are separately patentable because the Examiner fails to note where all of the claim elements are taught and suggested, and therefore, the requirements for a *prima facie* case of obviousness have not been met. Should claim 1 fall, claims 13, 14, and 15 are separately patentable and not obvious in light of Fick.

f) Claims 16 and 17 stand rejected under 35 U.S.C. §103(a)

The Examiner fails to note where in Fick the elements of Claims 16 and 17 are taught or suggested, and therefore fails to meet the requirements for a *prima facie* case of obviousness. Thus, these claims are separately patentable should claim 1 fall, and are not obvious in light of Fick.

g) Claim 126 stands rejected under 35 U.S.C. §103(a)

Claim 126 is separately patentable because the Examiner fails to note where each of the claim elements are taught or suggested in Fick. As such, the requirements for a *prima facie* case of obviousness are not met in this case. Should claim 1 fall, claim 126 is separately patentable and not obvious in light of Fick.

h) Claim 127 stands rejected under 35 U.S.C. §103(a)

The Examiner also fails to identify in Fick where all of the claim elements of Claim 127 are taught or suggested. Thus, a *prima facie* case of obviousness for this claim has not been met, and the claim is separately patentable from claim 1. In the event that claim 1 falls, claim 127 is separately patentable and not obvious in light of Fick.

i) Claim 128 stands rejected under 35 U.S.C. §103(a)

Claim 128 is separately patentable because the Examiner has failed to show where each of the claim elements have been taught or suggested in Fick. Therefore, the requirements for a *prima facie* case of obviousness are not met for this claim, and should claim 1 fall, claim 128 is separately patentable and not obvious in light of Fick.

VIII. CONCLUSION

Appellants have provided arguments that overcome the pending rejection. Appellants respectfully submit that the Office Action's conclusions that the claims should be rejected are unwarranted. It is therefore requested that the Board overturn the Action's rejections.

Please date stamp and return the enclosed postcard to evidence receipt of this document.

Dated: January 14, 2005

Respectfully submitted,

By _____

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APPENDIX 1

PENDING CLAIMS

1. (Previously Presented) A method of dispensing a therapeutic agent *in situ* to a localized region in an individual comprising administering to said region a polymer composition that comprises a biocompatible polymer, a cross-linking composition that comprises a cross-linker, and the therapeutic agent, wherein the biocompatible polymer and the cross-linking composition are administered to allow formation of a cross-linked polymer *in situ* at the localized region, which cross-linked polymer comprises the therapeutic agent, and wherein the biocompatible polymer and the cross-linking composition are administered to the localized region from separate containers, wherein a first container comprises the biocompatible polymer and a second container comprises the cross-linking composition.
2. (Previously Presented) The method of claim 1, wherein the biocompatible polymer comprises the therapeutic agent.
3. (Original) The method of claim 1, wherein the polymer composition and the cross-linking composition are separately administered to the localized region.
4. (Cancelled)
5. (Previously Presented) The method of claim 1, wherein the first and second containers are syringes.
6. (Cancelled)
7. (Cancelled)
8. (Previously Presented) The method of claim 3, wherein the separate administrations of said polymer composition and said cross-linking composition are by syringe.
9. (Previously Presented) The method of claim 1, wherein the polymer composition and cross-linking compositions are administered separately from a syringe having at least two compartments, said compartments further defined as said separate containers.
10. (Original) The method of claim 1, wherein the polymer is a polysaccharide, a polyamino acid polymer, or a combination thereof.

11. (Original) The method of claim 10, wherein the polymer is a polysaccharide, and the polysaccharide polymer is an alginate, hydroxycellulose, chondroitin, chitosan, hyaluronate, dextran, or starch.
12. (Original) The method of claim 10, wherein the polymer is a polyamino acid, and the polyamino acid is a polyglutamate or a polyaspartate.
13. (Original) The method of claim 1, wherein said cross-linking agent is a salt of a divalent cation.
14. (Previously Presented) The method of claim 13, wherein said divalent cation is Ca^{2+}, Mg^{2+}, Mn^{2+}, Cu^{2+}, Cr^{2+}, Sr^{2+}, Zn^{2+}, Ra^{2+}, Sn^{2+}, or Be^{2+}.
15. (Previously Presented) The method of claim 13, wherein said salt of a divalent cation is tin chloride, calcium chloride, calcium sulfate, calcium phosphate, calcium carbonate, calcium chlorate, calcium fluoride, calcium bromide, magnesium chloride, magnesium sulfate, magnesium phosphate, magnesium carbonate, magnesium chlorate, magnesium fluoride, magnesium bromide, manganese chloride, manganese sulfate, manganese phosphate, manganese carbonate, manganese chlorate, manganese fluoride, manganese bromide, copper chloride, copper sulfate, copper phosphate, copper carbonate, copper chlorate, copper fluoride, copper bromide, chromium chloride, chromium sulfate, chromium phosphate, chromium carbonate, chromium chlorate, chromium fluoride, chromium bromide, strontium chloride, strontium sulfate, strontium phosphate, strontium carbonate, strontium chlorate, strontium fluoride, strontium bromide, zinc chloride, zinc sulfate, zinc phosphate, zinc carbonate, zinc chlorate, zinc fluoride, zinc bromide, radium chloride, radium sulfate, radium phosphate, radium carbonate, radium chlorate, radium fluoride, radium bromide, beryllium chloride, beryllium sulfate, beryllium phosphate, beryllium carbonate, beryllium chlorate, beryllium fluoride, or beryllium bromide.
16. (Original) The method of claim 1, wherein the therapeutic agent is a drug, a hormone, a gene therapy composition, a radionuclide, a nutriceutical, or a combination thereof.
17. (Original) The method of claim 16, wherein the therapeutic agent is a drug, and the drug is cisplatin, doxorubicin, Taxol, daunorubicin, mitomycin, actinomycin D, bleomycin, VP16, tumor necrosis factor, vincristine, vinblastine, carmustine, melphalan, cyclophosphamide, chlorambucil, bisulfan, lomustine, penicillin, erythromycin, amoxicillin, cefazolin, imipenem, aztreonam, sulbactam, linezolid, gentamicin,

sulfamethoxazole, vancomycin, ciprofloxacin, fusidic acid, trimethoprim, metronidazole, clindamycin, mupirocin, amphotericin B, rifampin, fluconazoleor, or a combination thereof.

18. (Withdrawn) The method of claim 16, wherein the therapeutic agent is a hormone, and the hormone is luteinizing hormone releasing hormone, growth hormone, growth hormone releasing hormone, estrogen, progesterone, testosterone, androgen, corticotropin, prolactin, gonadotropin, somatotropin, somatostatin, somatotropin releasing hormone, gonadotropin releasing hormone, corticotropin releasing hormone, prolactin releasing hormone, pro-opiomelanocortin, melanotropin, calcitonin, gastrin, secretin, aldosterone, epinephrine, norepinephrine, follicle stimulating hormone, insulin, acetylcholine, aldosterone, angiotensin II, arginine vasopressin, bombesin, bradykinin, caerulein, calcitonin, cholecystokinin, chymodenin, corticosterone, cortisol, cortisone, dihydrotestosterone, dopamine, β-endorphin, epidermal growth factor, erythropoietin, estradiol, fibroblast growth factor, gamma aminobutyric acid, gastric inhibitory peptide, gastrin, glucagon, histamine, human chorionic gonadotropin, human placental lactogen, inhibin, insulinlike growth factor I, insulinlike growth factor II, leucine enkephalin, leukotrienes, lysine vasopressin, lysylbradykinin, melanin concentrating hormone, α-melanocyte stimulating hormone, mesotocin, methionin enkephalin, motilin, MSH release inhibiting factor, Mullerian regression factor, nerve growth factor, neurotensin, oxytocin, pancreatic polypeptide, parathormone, platelet-derived growth factor, prolactin inhibiting factor, prostacyclin I2, prostaglandin E2, prostaglandin F2a, relaxin, serotonin, serum thymic factor, substance P, thromboxane A2, thymopoietin, thymosina, thyrotopin (thyroid stimulating hormone; TSH), thyrotropin releasing hormone, thyroxine, triiodothyronine, urogastrone, vasoactive intestinal peptide, vasotocin, vitamin D3, or a combination thereof.

19. (Withdrawn) The method of claim 16, wherein the therapeutic agent is a gene therapy composition, and the gene therapy composition is a vector containing p53, thymidine kinase, cytosine deaminase, oxidoreductase, thymidine kinase thymidilate kinase, deoxycytidine kinase, *ras ; myc, raf, erb, src, fms, jun, trk, ret, gsp, hst, bcl abl,* Rb, CFTR, p16, p21, p27, p57, p73, C-CAM, APC, CTS-1, zac1, scFV *ras*, DCC, NF-1, NF-2, WT-1, MEN-I, MEN-II, BRCA1, VHL, MMAC1, FCC, MCC, BRCA2, IL-1, IL-2,

IL-3, IL-4, IL-5, IL-6, IL-7, IL-8, IL-9, IL-10, IL-11 IL-12, GM-CSF, G-CSF, or a combination thereof.

20. (Withdrawn) The method of claim 19, wherein the vector is a plasmid, an adenoviral vector, an adeno-associated viral vector, a retroviral vector, a liposome, or a combination thereof.

21. (Withdrawn) The method of claim 16, wherein the therapeutic agent is a radionuclide, and the radionuclide is ^{188}Re, ^{213}Bi, ^{166}Ho, ^{211}At, or a combination thereof.

22. (Withdrawn) The method of claim 16, wherein the therapeutic agent is a nutriceutical, and the nutriceutical is arabinogalactan, acerola cherry, agnus castus (vitex), amla, andrographis,artichoke (globe), ashwagandha, astragalus, bacopa, beta 1,3 glucans, beta sitosterol, bilberry, borage oil, boswellia, broccoli cruciferous, bromelain, butcher's broom, calcium hydroxyl apatite, cascara sagrada, cat's claw, cetyl myristoleate, chamomile, chitosan, chlorella, chondroitin sulfate, chromium yeast, citrus aurantium, citrus seed extract, co-enzyme Q10, colostrum, cordyceps, cranberry, creatine monohydrate, devil's claw, DHEA, DMG, dong quai, echinacea, elderberry, ephedra, evening primrose oil, feverfew, fish marine lipids, fish oil concentrate powder, fish protein powder, flaxseed oil, garcinia HCA, garlic T.A.P., germanium Ge-132, ginger, ginkgo, ginseng-American, ginseng-Siberian, ginseng-Asian, glucosamine, goldenseal, gotu kola, grapeseed extract, green tea extract, guarana, gymnema, hawthorne, hops, horse chestnut, horsetail, kava kava, kola nut, lecithin,licorice, lipoic acid, lycopene, medium chain tri-glycerides, melatonin, milk thistle, MSM, muira puama, nag, nettles, noni, ocimum sanctum, octacosonol, olivir, passion flower, pau d'arcophosphatidylserine, picrorhiza, potassium glycero phosphate, pygeum, quercetin, reishi, saw palmetto, schisandra, sea cucumber, selenium yeast bound, shark cartilage, shark liver oil, shiitake, shilajit, sodium copper chlorophyllin, spirulina, squalene, St. John's Wort, stevia, suma, tribulus (Bulgarian) triphala, tumeric, uva ursi, valerian, wild yam extract, willow bark, yohimbe bark extract, or a combination thereof.

23. (Cancelled)

24. (Withdrawn) A method of treating a tumor *in situ* in an individual comprising the steps of administering to said tumor a polymer composition that comprises a biocompatible polymer, a cross-linking composition that comprises a cross-linker, and the therapeutic

agent, wherein the polymer composition and the cross-linking composition are administered to allow formation of a cross-linked polymer *in situ* at the tumor, which cross-linked polymer comprises the therapeutic agent.

25. (Withdrawn) The method of claim 24, wherein the polymer composition comprises the therapeutic agent.
26. (Withdrawn) The method of claim 24, wherein the polymer composition and the cross-linking composition are separately administered to the localized region.
27. (Withdrawn) The method of claim 26, wherein the polymer composition and the cross-linking composition are administered to the localized region from separate containers, wherein a first container contains the polymer composition and a second container comprises the cross-linking composition.
28. (Withdrawn) The method of claim 27, wherein the first and second containers are syringes.
29. (Withdrawn) The method of claim 24, wherein the polymer composition and the cross-linking composition are administered to said region by means of a single container having at least two compartments, wherein one compartment comprises the polymer composition and another compartment comprises the cross-linking composition.
30. (Withdrawn) The method of claim 24, wherein the polymer composition and the cross-linking composition are administered to said region by means of a single container having a hollow cylindrical compartment, wherein the polymer composition and cross-linking composition are administered separately through said compartment.
31. (Withdrawn) The method of claim 30, wherein the separate administrations of said polymer composition and said cross-linking composition are by syringe.
32. (Withdrawn) The method of claim 24, wherein the polymer composition and cross-linking compositions are administered separately from a syringe having at least two compartments.
33. (Withdrawn) The method of claim 24, wherein the polymer is a polysaccharide, a polyamino acid polymer, or a combination thereof.
34. (Withdrawn) The method of claim 33, wherein the polymer is a polysaccharide, and the polysaccharide polymer is an alginate, hydroxycellulose, chondroitin, chitosan, hyaluronate, dextran or starch.

35. (Withdrawn) The method of claim 33, wherein the polymer is a polyamino acid, and the polyamino acid is a polyglutamate or a polyaspartate.

36. (Withdrawn) The method of claim 24, wherein said cross-linking agent is a salt of a divalent cation.

37. (Withdrawn) The method of claim 36, wherein said divalent cation is Ca^{2+}, Mg^{2+}, Mn^{2+}, Cu^{2+}, Cr^{2+}, Sr^{2+}, Zn^{2+}, Ra^{2+}, or Be2+.

38. (Withdrawn) The method of claim 36, wherein said salt of a divalent cation is calcium chloride, calcium sulfate, calcium phosphate, calcium carbonate, calcium chlorate, calcium fluoride, calcium bromide, magnesium chloride, magnesium sulfate, magnesium phosphate, magnesium carbonate, magnesium chlorate, magnesium fluoride, magnesium bromide, manganese chloride, manganese sulfate, manganese phosphate, manganese carbonate, manganese chlorate, manganese fluoride, manganese bromide, copper chloride, copper sulfate, copper phosphate, copper carbonate, copper chlorate, copper fluoride, copper bromide, chromium chloride, chromium sulfate, chromium phosphate, chromium carbonate, chromium chlorate, chromium fluoride, chromium bromide, strontium chloride, strontium sulfate, strontium phosphate, strontium carbonate, strontium chlorate, strontium fluoride, strontium bromide, zinc chloride, zinc sulfate, zinc phosphate, zinc carbonate, zinc chlorate, zinc fluoride, zinc bromide, radium chloride, radium sulfate, radium phosphate, radium carbonate, radium chlorate, radium fluoride, radium bromide, beryllium chloride, beryllium sulfate, beryllium phosphate, beryllium carbonate, beryllium chlorate, beryllium fluoride, or beryllium bromide.

39. (Withdrawn) The method of claim 24, wherein said therapeutic agent is a drug, a hormone, a gene therapy composition, a radionuclide, a nutriceutical, or a combination thereof.

40. (Withdrawn) The method of claim 39, wherein the therapeutic agent is a drug, and the drug is cisplatin, doxorubicin, Taxol, daunorubicin, mitomycin, actinomycin D, bleomycin, VP16, tumor necrosis factor, vincristine, vinblastine, carmustine, melphalan, cyclophosphamide, chlorambucil, bisulfan, lomustine, penicillin, erythromycin, amoxicillin, cefazolin, imipenem, aztreonam, sulbactam, linezolid, gentamicin, sulfamethoxazole, vancomycin, ciprofloxacin, fusidic acid, trimethoprim, metronidazole,

clindamycin, mupirocin, amphotericin B, rifampin, fluconazoleor, or a combination thereof.

41. (Withdrawn) The method of claim 39, wherein the therapeutic agent is a hormone, and the hormone is luteinizing hormone releasing hormone, growth hormone, growth hormone releasing hormone, estrogen, progesterone, testosterone, androgen, corticotropin, prolactin, gonadotropin, somatotropin, somatostatin, somatotropin releasing hormone, gonadotropin releasing hormone, corticotropin releasing hormone, prolactin releasing hormone, pro-opiomelanocortin, melanotropin, calcitonin, gastrin, secretin, aldosterone, epinephrine, norepinephrine, follicle stimulating hormone, insulin, acetylcholine, aldosterone, angiotensin II, arginine vasopressin, bombesin, bradykinin, caerulein, calcitonin, cholecystokinin, chymodenin, corticosterone, cortisol, cortisone, dihydrotestosterone, dopamine, β-endorphin, epidermal growth factor, erythropoietin, estradiol, fibroblast growth factor, gamma aminobutyric acid, gastric inhibitory peptide, gastrin, glucagon, histamine, human chorionic gonadotropin, human placental lactogen, inhibin, insulinlike growth factor I, insulinlike growth factor II, leucine enkephalin, leukotrienes, lysine vasopressin, lysylbradykinin, melanin concentrating hormone, α-melanocyte stimulating hormone, mesotocin, methionin enkephalin, motilin, MSH release inhibiting factor, Mullerian regression factor, nerve growth factor, neurotensin, oxytocin, pancreatic polypeptide, parathormone, platelet-derived growth factor, prolactin inhibiting factor, prostacyclin I2, prostaglandin E2, prostaglandin F2a, relaxin, serotonin, serum thymic factor, substance P, thromboxane A2, thymopoietin, thymosina, thyrotopin (thyroid stimulating hormone; TSH), thyrotropin releasing hormone, thyroxine, triiodothyronine, urogastrone, vasoactive intestinal peptide, vasotocin, vitamin D3, or a combination thereof.

42. (Withdrawn) The method of claim 39, wherein the therapeutic agent is a gene therapy composition, and the gene therapy composition is a vector containing p53, thymidine kinase, cytosine deaminase, oxidoreductase, thymidine kinase thymidilate kinase, deoxycytidine kinase, *ras ; myc, raf, erb, src, fms, jun, trk, ret, gsp, hst, bcl abl*, Rb, CFTR, p16, p21, p27, p57, p73, C-CAM, APC, CTS-1, zac1, scFV *ras*, DCC, NF-1, NF-2, WT-1, MEN-I, MEN-II, BRCA1, VHL, MMAC1, FCC, MCC, BRCA2, IL-1, IL-2,

IL-3, IL-4, IL-5, IL-6, IL-7, IL-8, IL-9, IL-10, IL-11 IL-12, GM-CSF, G-CSF, or a combination thereof.

43. (Withdrawn) The method of claim 42, wherein the vector is a plasmid, an adenoviral vector, an adeno-associated viral vector, a retroviral vector, a liposome, or a combination thereof.

44. (Withdrawn) The method of claim 39, wherein the therapeutic agent is a radionuclide, and the radionuclide is ^{188}Re, ^{213}Bi, ^{166}Ho, ^{211}At, or a combination thereof.

45. (Withdrawn) The method of claim 39, wherein the therapeutic agent is a nutriceutical, and the nutriceutical is arabinogalactan, acerola cherry, agnus castus (vitex), amla, andrographis,artichoke (globe), ashwagandha, astragalus, bacopa, beta 1,3 glucans, beta sitosterol, bilberry, borage oil, boswellia, broccoli cruciferous, bromelain, butcher's broom, calcium hydroxyl apatite, cascara sagrada, cat's claw, cetyl myristoleate, chamomile, chitosan, chlorella, chondroitin sulfate, chromium yeast, citrus aurantium, citrus seed extract, co-enzyme Q10, colostrum, cordyceps, cranberry, creatine monohydrate, devil's claw, DHEA, DMG, dong quai, echinacea, elderberry, ephedra, evening primrose oil, feverfew, fish marine lipids, fish oil concentrate powder, fish protein powder, flaxseed oil, garcinia HCA, garlic T.A.P., germanium Ge-132, ginger, ginkgo, ginseng-American, ginseng-Siberian, ginseng-Asian, glucosamine, goldenseal, gotu kola, grapeseed extract, green tea extract, guarana, gymnema, hawthorne, hops, horse chestnut, horsetail, kava kava, kola nut, lecithin,licorice, lipoic acid, lycopene, medium chain tri-glycerides, melatonin, milk thistle, MSM, muira puama, nag, nettles, noni, ocimum sanctum, octacosonol, olivir, passion flower, pau d'arcophosphatidylserine, picrorhiza, potassium glycero phosphate, pygeum, quercetin, reishi, saw palmetto, schisandra, sea cucumber, selenium yeast bound, shark cartilage, shark liver oil, shiitake, shilajit, sodium copper chlorophyllin, spirulina, squalene, St. John's Wort, stevia, suma, tribulus (Bulgarian) triphala, tumeric, uva ursi, valerian, wild yam extract, willow bark, yohimbe bark extract, or a combination thereof.

46. (Cancelled).

47. (Withdrawn) A method of occluding an artery associated with a tumor in an individual comprising the step of administering to said tumor a polymer composition that comprises a biocompatible polymer, a cross-linking composition that comprises a cross-linker,

wherein the polymer composition and the cross-linking composition are administered to allow formation of the cross-linked polymer *in situ* at the tumor.

48. (Withdrawn) The method of claim 47, wherein the polymer composition further comprises a therapeutic agent.

49. (Withdrawn) The method of claim 47, wherein the polymer composition and the cross-linking composition are separately administered to the tumor.

50. (Withdrawn) The method of claim 49, wherein the polymer composition and the cross-linking composition are administered to the tumor from separate containers, wherein a first container contains the polymer composition and a second container comprises the cross-linking composition.

51. (Withdrawn) The method of claim 50, wherein the first and second containers are syringes.

52. (Withdrawn) The method of claim 47, wherein the polymer composition and the cross-linking composition are administered to the tumor by means of a single container having at least two compartments, wherein one compartment comprises the polymer composition and another compartment comprises the cross-linking composition.

53. (Withdrawn) The method of claim 47, wherein the polymer composition and the cross-linking composition are administered to said region by means of a single container having a hollow cylindrical compartment, wherein the polymer composition and cross-linking composition are administered separately through said compartment.

54. (Withdrawn) The method of claim 53, wherein the separate administrations of said polymer composition and said cross-linking composition are by syringe.

55. (Withdrawn) The method of claim 47, wherein the polymer composition and cross-linking compositions are administered separately from a syringe having at least two compartments.

56. (Withdrawn) The method of claim 47, wherein the polymer is a polysaccharide, a polyamino acid polymer, or a combination thereof.

57. (Withdrawn) The method of claim 56, wherein the polymer is a polysaccharide, and the polysaccharide polymer is an alginate, hydroxycellulose, chondroitin, chitosan, hyaluronate, dextran or starch.

58. (Withdrawn) The method of claim 56, wherein the polymer is a polyamino acid, and the polyamino acid is a polyglutamate or a polyaspartate.

59. (Withdrawn) The method of claim 47, wherein said cross-linking agent is a salt of a divalent cation.

60. (Withdrawn) The method of claim 59, wherein said divalent cation is Ca^{2+}, Mg^{2+}, Mn^{2+}, Cu^{2+}, Cr^{2+}, Sr^{2+}, Zn^{2+}, Ra^{2+}, Sn^{2+}, or Be^{2+}.

61. (Withdrawn) The method of claim 59, wherein said salt of a divalent cation is calcium chloride, calcium sulfate, calcium phosphate, calcium carbonate, calcium chlorate, calcium fluoride, calcium bromide, magnesium chloride, magnesium sulfate, magnesium phosphate, magnesium carbonate, magnesium chlorate, magnesium fluoride, magnesium bromide, manganese chloride, manganese sulfate, manganese phosphate, manganese carbonate, manganese chlorate, manganese fluoride, manganese bromide, copper chloride, copper sulfate, copper phosphate, copper carbonate, copper chlorate, copper fluoride, copper bromide, chromium chloride, chromium sulfate, chromium phosphate, chromium carbonate, chromium chlorate, chromium fluoride, chromium bromide, strontium chloride, strontium sulfate, strontium phosphate, strontium carbonate, strontium chlorate, strontium fluoride, strontium bromide, zinc chloride, zinc sulfate, zinc phosphate, zinc carbonate, zinc chlorate, zinc fluoride, zinc bromide, radium chloride, radium sulfate, radium phosphate, radium carbonate, radium chlorate, radium fluoride, radium bromide, beryllium chloride, beryllium sulfate, beryllium phosphate, beryllium carbonate, beryllium chlorate, beryllium fluoride, or beryllium bromide.

62. (Withdrawn) The method of claim 47, wherein said therapeutic agent is a drug, a hormone, a gene therapy composition, a radionuclide, a nutriceutical, or a combination thereof.

63. (Withdrawn) The method of claim 62, wherein the therapeutic agent is a drug, and the drug is cisplatin, doxorubicin, Taxol, daunorubicin, mitomycin, actinomycin D, bleomycin, VP16, tumor necrosis factor, vincristine, vinblastine, carmustine, melphalan, cyclophosphamide, chlorambucil, bisulfan, lomustine, penicillin, erythromycin, amoxicillin, erythromycin, cefazolin, imipenem, aztreonam, sulbactam, linezolid, gentamicin, sulfamethoxazole, vancomycin, ciprofloxacin, fusidic acid, trimethoprim,

metronidazole, clindamycin, mupirocin, amphotericin B, rifampin, fluconazoleor, or a combination thereof.

64. (Withdrawn) The method of claim 62, wherein the therapeutic agent is a hormone, and the hormone is luteinizing hormone releasing hormone, growth hormone, growth hormone releasing hormone, estrogen, progesterone, testosterone, androgen, corticotropin, prolactin, gonadotropin, somatotropin, somatostatin, somatotropin releasing hormone, gonadotropin releasing hormone, corticotropin releasing hormone, prolactin releasing hormone, pro-opiomelanocortin, melanotropin, calcitonin, gastrin, secretin, aldosterone, epinephrine, norepinephrine, follicle stimulating hormone, insulin, acetylcholine, aldosterone, angiotensin II, arginine vasopressin, bombesin, bradykinin, caerulein, calcitonin, cholecystokinin, chymodenin, corticosterone, cortisol, cortisone, dihydrotestosterone, dopamine, β-endorphin, epidermal growth factor, erythropoietin, estradiol, fibroblast growth factor, gamma aminobutyric acid, gastric inhibitory peptide, gastrin, glucagon, histamine, human chorionic gonadotropin, human placental lactogen, inhibin, insulinlike growth factor I, insulinlike growth factor II, leucine enkephalin, leukotrienes, lysine vasopressin, lysylbradykinin, melanin concentrating hormone, α-melanocyte stimulating hormone, mesotocin, methionin enkephalin, motilin, MSH release inhibiting factor, Mullerian regression factor, nerve growth factor, neurotensin, oxytocin, pancreatic polypeptide, parathormone, platelet-derived growth factor, prolactin inhibiting factor, prostacyclin I2, prostaglandin E2, prostaglandin F2a, relaxin, serotonin, serum thymic factor, substance P, thromboxane A2, thymopoietin, thymosina, thyrotopin (thyroid stimulating hormone; TSH), thyrotropin releasing hormone, thyroxine, triiodothyronine, urogastrone, vasoactive intestinal peptide, vasotocin, vitamin D3, or a combination thereof.

65. (Withdrawn) The method of claim 62, wherein the therapeutic agent is a gene therapy composition, and the gene therapy composition is a vector containing p53, thymidine kinase, cytosine deaminase, oxidoreductase, thymidine kinase thymidilate kinase, deoxycytidine kinase, *ras ; myc, raf, erb, src, fms, jun, trk, ret, gsp, hst, bcl abl*, Rb, CFTR, p16, p21, p27, p57, p73, C-CAM, APC, CTS-1, zac1, scFV *ras*, DCC, NF-1, NF-2, WT-1, MEN-I, MEN-II, BRCA1, VHL, MMAC1, FCC, MCC, BRCA2, IL-1, IL-2,

IL-3, IL-4, IL-5, IL-6, IL-7, IL-8, IL-9, IL-10, IL-11 IL-12, GM-CSF, G-CSF, or a combination thereof.

66. (Withdrawn) The method of claim 65, wherein the vector is a plasmid, an adenoviral vector, an adeno-associated viral vector, a retroviral vector, a liposome, and a combination thereof.

67. (Withdrawn) The method of claim 62, wherein the therapeutic agent is a radionuclide, and the radionuclide is ^{188}Re, ^{213}Bi, ^{166}Ho, ^{211}At, or a combination thereof.

68. (Withdrawn) The method of claim 62, wherein the therapeutic agent is a nutriceutical, and the nutriceutical is arabinogalactan, acerola cherry, agnus castus (vitex), amla, andrographis,artichoke (globe), ashwagandha, astragalus, bacopa, beta 1,3 glucans, beta sitosterol, bilberry, borage oil, boswellia, broccoli cruciferous, bromelain, butcher's broom, calcium hydroxyl apatite, cascara sagrada, cat's claw, cetyl myristoleate, chamomile, chitosan, chlorella, chondroitin sulfate, chromium yeast, citrus aurantium, citrus seed extract, co-enzyme Q10, colostrum, cordyceps, cranberry, creatine monohydrate, devil's claw, DHEA, DMG, dong quai, echinacea, elderberry, ephedra, evening primrose oil, feverfew, fish marine lipids, fish oil concentrate powder, fish protein powder, flaxseed oil, garcinia HCA, garlic T.A.P., germanium Ge-132, ginger, ginkgo, ginseng-American, ginseng-Siberian, ginseng-Asian, glucosamine, goldenseal, gotu kola, grapeseed extract, green tea extract, guarana, gymnema, hawthorne, hops, horse chestnut, horsetail, kava kava, kola nut, lecithin,licorice, lipoic acid, lycopene, medium chain tri-glycerides, melatonin, milk thistle, MSM, muira puama, nag, nettles, noni, ocimum sanctum, octacosonol, olivir, passion flower, pau d'arcophosphatidylserine, picrorhiza, potassium glycero phosphate, pygeum, quercetin, reishi, saw palmetto, schisandra, sea cucumber, selenium yeast bound, shark cartilage, shark liver oil, shiitake, shilajit, sodium copper chlorophyllin, spirulina, squalene, St. John's Wort, stevia, suma, tribulus (Bulgarian) triphala, tumeric, uva ursi, valerian, wild yam extract, willow bark, yohimbe bark extract, or a combination thereof.

69. (Cancelled).

70. (Withdrawn) The method of claim 47, wherein said administration step occurs through a catheter.

71. -125. (Cancelled).

126. (Previously Presented) A method of dispensing a therapeutic agent *in situ* to a localized region in an individual comprising administering to said region a polymer composition that comprises a biocompatible polymer, a cross-linking composition that comprises a cross-linker, and the therapeutic agent, wherein the polymer composition and the cross-linking composition are administered to allow formation of a cross-linked polymer *in situ* at the localized region, which cross-linked polymer comprises the therapeutic agent, wherein the polymer composition and the cross-linking composition are separately administered to the localized region by means of a single container having at least two compartments, wherein one compartment comprises the polymer composition and another compartment comprises the cross-linking composition.

127. (Previously Presented) A method of dispensing a therapeutic agent *in situ* to a localized region in an individual comprising administering to said region a polymer composition that comprises a biocompatible polymer, a cross-linking composition that comprises a cross-linker, and the therapeutic agent, wherein the polymer composition and the cross-linking composition are administered to allow formation of a cross-linked polymer *in situ* at the localized region, which cross-linked polymer comprises the therapeutic agent, wherein the polymer composition and the cross-linking composition are separately administered to the localized region by means of a single container having a hollow cylindrical compartment, wherein the polymer composition and cross-linking composition are administered separately through said compartment.

128. (Previously Presented) The method of claim 1, wherein said administration is to a tumor.

APPENDIX 2

EVIDENCE APPENDIX

1. U.S. Patent No. 5,945,100-Cited by the Examiner in Office Action mailed July 15, 2003
2. U.S. Patent No. 5,989,215-Cited by the Examiner in Office Action mailed February 24, 2004